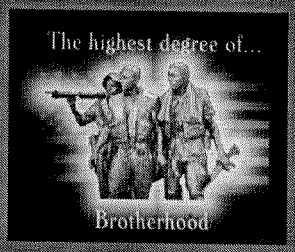
May/June 2002

Editor:
Jean Eilertson, PharmD



The Apothecary Bulletin

PHARMACY SERVICE & THERAPEUTICS COMMITTEES
US ARMY MEDDAC, FORT CARSON, COLORADO

FORMULARY CHANGES

The Pikes Peak Region Formulary Committee met on 2 May 2002 and the Evans Pharmacy & Therapeutics (P&T) Committee met on 14 May 2002 with the following medications ***added*** to the Formulary:

+ dextroamphetamine/amphetamine 10mg, 20mg, and 30mg extended release capsules (*Adderall XR*)
+ guaifenesin/pseudoephedrine sprinkles (*Guaifed PD*) — **for use in patients unable to swallow Entex PSE tablets**

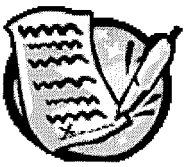
No medications were ***deleted*** from the Formulary.

The Pikes Peak Region Formulary Committee reviewed the oral anti-infective agents - no changes were made to the Formulary. As part of this ongoing drug class review process, the Committee (with representatives from the Air Force Academy, Peterson AFB, and Evans) will conduct reviews as follows:

July 2002 (meeting will be 27 June) = cardiovascular agents
September 2002 = endocrine/hematologic agents
November 2002 = gastrointestinal/renal/genitourinary agents
January 2003 = central nervous system agents
March 2003 = dermatologic/ophthalmologic agents

Pharmaceuticals submitted for Formulary consideration will be reviewed based on the above schedule. If a medication is a new entity, it may be considered earlier if submitted via a New Drug Request. Providers desiring to have input into the drug class reviews are encouraged to contact one of the Pikes Peak Committee members: **LTC Edward Torkilson (Pharmacy), MAJ Robert Gray (Family Practice), and Dr. Garold Paul (Internal Medicine).**

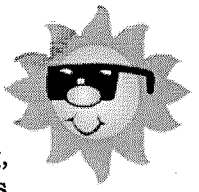
The next Formulary Committee Meetings will be held on Thursday, 27 June (Pikes Peak), and Tuesday, 9 July (Evans' P&T). New Drug Requests must be received by the Chief, Pharmacy Service, no later than **19 June** to be considered at the next meetings.



Dr. Steve Lang, Family Practice Clinic, has composed a memorandum regarding the alternating of antipyretics (ibuprofen and acetaminophen) in children with fevers. The memo has been approved by COL Dai, Chief of Pediatrics, and COL Solano, Chief of Primary Care Careline, and can be found at **Enclosure 1**.

"Every Memorial Day, we try to grasp the extent of this loss and the meaning of this sacrifice. And it always seems more than words can convey. All we can do is remember and always appreciate the price that was paid for our own lives and for our own freedom."
— President George W. Bush, Memorial Day, 2001

Q & A



Now that Spring is here and Summer is fast approaching, which medications can cause photosensitivity and what recommendations can be made to patients to minimize the risk of this adverse event?

see page 3

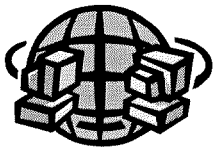
In this issue....

PDTS — IT'S MORE THAN A 4-LETTER WORD

A little over a year ago, **PDTS (Pharmacy Data Transaction Service)** was launched (or inflicted) upon this facility. At that time the only thing the providers and the pharmacy staff got from it was a delay in processing prescription entry. Since that time, the entire military health system (MHS) has been brought on-line with this program.

At last, there is finally some benefit to our patients and to us. Anytime a patient obtains a prescription at a MTF, a network pharmacy, or the National Mail Order Pharmacy (NMOP), the new prescription is screened against the patient's *full* medication profile. This prevents drug interactions, duplication of therapy, as well as overuse of medication. Until recently, all you received was a warning of possible problems, without being able to see exactly what that problem was.

Now, with the last CHCS upgrade, we have the ability to **look at a patient's full medication profile extending back 6 months.** This means that providers can now look at what a patient **has received at government expense** during that time frame, provided it was filled in one of the mentioned pharmacies.



To display this extended profile, follow these steps:

- In the **ORE** function at the **ACTION:** prompt, type **DPRX** and hit ENTER.
- Select the timeframe you wish to look at (type in the corresponding number – 1,2,3,4,5) and hit ENTER.
- CHCS will then ask if you want it sent to your mailbox. The choice is yours. I prefer to have it on the screen without going to the mailbox. **It takes about 20 seconds for the full profile to appear.** Medications entered in CHCS appear first, followed by those filled in either a network pharmacy or the NMOP. Use the arrow key to scroll down to view what the patient got, when they got it, the quantity, as well as where it was filled and who prescribed it.

The Pharmacy uses this tool to ensure no harm may come to the patient from a drug interaction as well as using it to identify patients misusing or overusing controlled substances.

If you have any questions, please **contact LTC Torkilson at 526-7334.**

New STD Guidelines

The CDC has published the fifth edition of their *Sexually Transmitted Diseases Treatment Guidelines*, discussing the assessment of patients' risk factors for STDs, the counseling of patients about contraceptives, and the effective treatment of infections. The Guidelines focus on chlamydia screening, screening strategies for men who have sex with men, and issues regarding region-specific drug-resistant gonorrhea. The Guidelines can be found at:

www.cdc.gov/std

New FDA Approvals

- *Lipitor* (atorvastatin) — new recommended starting doses of 10mg, 20mg, or 40mg; 40mg dose recommended for patients who require LDL reduction of more than 45%
- *Faslodex* (fulvestrant) — for the treatment of hormone receptor positive metastatic breast cancer in postmenopausal women with disease progression following antiestrogen therapy

Drug Interaction Corner

Many drugs interact with warfarin (*Coumadin*), and the list keeps growing. References list as many as 100 drugs that can create problems. Below is a partial list of drugs that may interact with warfarin:

May potentiate warfarin by either inhibition of metablism, diplacement from binding sites, interference with vitamin K, or effects on platelet function:

acetaminophen
amiodarone
beta blockers
cephalosporins
cimetidine
chloral hydrate
erythromycin
fluconazole
isoniazid
metronidazole
omeprazole
phenytoin
propafenone
qinidine
quinolones
sulfinpyrazone
tetracyclines
TMP/SMX (*Bactrim, Septra*)

May inhibit warfarin by either induction of hepatic enzymes or various other mechanisms:

barbiturates
carbamazepine
cholestyramine
dicloxacillin
griseofulvin
nafcillin
rifampin
sucralfate

Can contribute to bleeding problems:

aspirin and other NSAIDs
heparin

Herbal products that may interact:

Bilberry, Chamomile, Devil's Claw, Dong Quai, Fenugreek, Garlic, Ginger, Ginkgo Biloba, Ginseng, Horse Chestnut, Ma Huang, St. John's Wort

Q & A

Photosensitivity is a general term that describes either the common PHOTOTOXIC RESPONSE or the uncommon PHOTOALLERGIC REACTION. The differences between these 2 types of photosensitivity reactions are based on the mechanism of action, the onset of rash, and the clinical presentation. Phototoxic reactions are nonimmunologic and resemble a sunburn. In comparison, photoallergic reactions are immunologic and require previous exposure to the photosensitizing agent. The initial eruption caused by a phototoxic reaction appears within 30 minutes up to hours after exposure to light energy (i.e., sunlight, filtered light, or artificial light). In comparison, photoallergic reactions appear 1 to 14 days after exposure to light energy. Patients who experience a photoxic reaction may present with erythema, pain, and edema (usually limited to exposed areas). Patients who experience photoallergic reactions may present with papulovesicular eruptions, pruritus, and eczematous dermatitis (may extend beyond exposed areas). Treatment consists of burn care and avoidance of the offending agent for phototoxic reactions. Antihistamines and steroids may be required for photoallergic reactions. **Source: *Micromedex***

The following is a **PARTIAL** list of medications or classes of medications that may cause photosensitivity (drug classes in upper case):

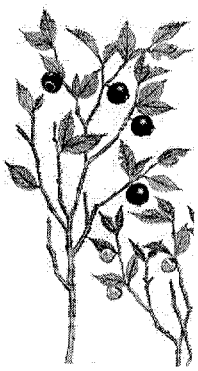
Antiacne agents — benzoyl peroxide, isotretinoin, tretinoin
Anticonvulsants — carbamazepine, gabapentin, phenytoin, valproic acid
Antidepressants — SSRIs, trazodone, TRICYCLICS
Antihistamines — brompheniramine, chlorpheniramine, cyproheptadine, diphenhydramine, loratidine
Antimicrobials — azithromycin, erythromycin, griseofulvin, QUINOLONES, SULFONAMIDES, TETRACYCLINES, trimethoprim
Antineoplastics — fluorouracil, flutamide, methotrexate, vinblastine
Antiparasitics — chloroquine, mefloquine, thiabendazole, quinine
Antipsychotics — haloperidol, PHENOTHIAZINES, olanzapine, risperidone, thiothixene
Cardiovasculars — ACE INHIBITORS, amiodarone, diltiazem, disopyramide, HMG-CoA-REDUCTASE INHIBITORS, losartan, methyldopa, minoxidil, nifedipine, quinidine
Diuretics — acetazolamide, amiloride, furosemide, metolazone, THIAZIDES, triamterene
Gastrointestinal agents — mesalamine, olsalazine, sulfasalazine
Herbal/Organic agents — Dong Quai, Gotu Kola, St. John's Wort
Other classes — BARBITURATES, ESTROGENS, SALICYLATES, SULFONYLUREAS, NSAIDs, ORAL CONTRACEPTIVES
Miscellaneous — amantadine, coal tar, gold salts, interferon beta-1b, isoniazide, pseudoephedrine, selegiline, vitamin A

The photoreaction depends on the patient, the amount of drug, and the length of time exposed to sunlight. Persons at risk should wear protective clothing (broad-rimmed hats, long sleeves and pants), use a good sunscreen (*minimum* SPF of 15, reapply every 2 hours and more frequently after swimming, sweating, or toweling), and avoid prolonged exposure to sunlight (particularly between 10 a.m. and 3 p.m.).

MedWatch Drug Warnings — for more information: www.fda.gov/medwatch/safety.htm

- a warning of the potential risk of severe liver injury (including hepatitis, cirrhosis, and liver failure) associated with the use of **kava-containing dietary supplements**
- changes to prescribing information for ***Vioxx* (rofecoxib)** based on the results of the VIGOR (*Vioxx* Gastrointestinal Outcomes Research) study which compared *Vioxx* 50mg daily with naproxen 500mg twice daily
  - information on the lower incidence of serious upper GI adverse events of major bleeding, perforation, and obstruction with *Vioxx* compared to naproxen
  - findings of a higher cumulative rate of serious cardiovascular thromboembolic adverse events (such as heart attacks, angina, and peripheral vascular events) in the *Vioxx* group (1.8%) compared to the naproxen group (0.6%) — data from two smaller studies comparing *Vioxx* 25mg daily with placebo did **not** show a difference in the rate of serious cardiovascular thromboembolic events; new labeling information will advise doctors to use caution in prescribing *Vioxx* for patients with ischemic heart disease and notes that *Vioxx* 50mg is not recommended for chronic use
- changes to prescribing information for ***Actos* (pioglitazone)** and ***Avandia* (rosiglitazone)** strengthening information on the possibility of fluid retention when either drug is used as monotherapy or in combination with insulin which may lead to, or exacerbate, CHF
- a change to the prescribing information for ***Geodon* (ziprasidone)** strengthening the warning not to use with any drugs *"that have demonstrated QT prolongation as one of their pharmacodynamic effects..."*
- postmarketing reports describing serious thrombotic events (vascular occlusion) possibly associated with the administration of **Immune Globulin Intravenous (Human)**
- a Black Box warning for **Lioresal Intrathecal** informing of rare cases of intrathecal baclofen withdrawal that can lead to life threatening sequelae and/or death in patients who abruptly discontinue therapy

HERB OF THE (every other) MONTH



Bilberry (*vaccinium myrtillus*), related to the blueberry, is a small, wild, perennial European berry shrub that is now cultivated from the Far East to the Unites States. Used by European herbalists for centuries, it has been used for diarrhea and stomach problems (the berries were mixed with honey and made into a syrup called *rob* in Elizabethan times), for infections, for scurvy, and for kidney stones. Saint Hildegard of Bingen (1098-1179) recommended the plant for inducing menstruation. In the 16th century, German herbalists recommended the berries for treatment of bladder stones, liver disorders, and in syrups for coughs and lung ailments. In the 18th century, use among herbalists and German physicians became widespread, with berry preparations used for various intestinal conditions, as well as typhoid fever, infections of the mouth and urinary tract, along with use in gout and rheumatism. Probably its most famous use was by the British Royal Air Force pilots during World War II who discovered that eating bilberry jam before night missions greatly improved their night vision. The leaves of the shrub, primarily used in the form of a tea, have been used for astringent, tonic, antiseptic, and anti-inflammatory qualities and were used as a folk remedy for diabetes.

Bilberries contain the antioxidants anthocyanosides. Bilberry extracts contain approximately 25% anthocyanosides, 1.5%-10% tannins, and small percentages of flavonoids, plant acids, and pectins. The anthocyanosides are thought to be the active components, producing reductions in vascular permeability and tissue edema in some animals. It is also thought to aid microvascular blood flow by intensifying arteriolar rhythmic diameter changes. Leaf extracts reduced triglyceride levels in diabetic rats immediately after feeding, possibly through increased triglyceride lipoprotein catabolism. Additionally, studies with animals have shown that anthocyanosides speed up regeneration of visual purple in the retina, allowing better adaptation to darkness and light. The anthocyanoside myrtillin causes hypoglycemia, although the mechanism is unclear.

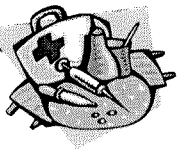
Bilberry is most commonly used as a component of treatment for various vision and eye disorders including glaucoma, cataracts, and macular degeneration. It has also been included in the treatments for many types of retinopathy and used for eye fatigue, poor night vision, and nearsightedness. In addition, it has been used to treat varicose veins and hemorrhoids. The German Commission E (regulates herbal use in Germany) classifies bilberry *fruit* as an approved herb for use in nonspecific, acute diarrhea and as local therapy for mild inflammation of the mucous membranes of the mouth and throat. In contrast, the German Commission E classifies bilberry *leaf* as an unapproved herb, stating "*since the efficacy has not been documented, a therapeutic use of bilberry leaf preparation is not justifiable in view of the risks involved*" (see paragraph on adverse effects).

Bilberry supplements are available as capsules and liquid extracts which should be a standardized formula of up to 25% anthocyanocides. Recommended doses are 60mg to 120mg of bilberry extract daily to improve night vision and 240mg to 480mg daily in 2 or 3 divided doses for visual and circulatory problems. It may be taken with or without food.

Bilberry fruit may be taken in large doses without any side effects. However, the leaves should not be taken in large doses or over long periods of time because they are toxic. Symptoms of chronic intoxication in animal experiments include cachexia, anemia, and acute excitation; continued chronic administration may be fatal. Use of bilberry with anticoagulants or antiplatelet agents may result in inhibition of platelet aggregation, potentially enhancing the risk of bleeding. Some herbal preparations contain alcohol and may result in a disulfiram-reaction if used concurrently with disulfiram. Bilberry is contraindicated in pregnant and breast-feeding patients.

Resources: *Complementary & Alternative Medicines* (1999), *The Review of Natural Products* (1995), Various Websites

ADVERSE DRUG REACTION REPORT



There were 58 adverse drug reactions (ADRs) documented for March (n=36) and April (n=22), of which 27 (47%) were reported **spontaneously** (7 each from Family Practice and Internal Medicine; 5 from PACC; 2 from Pediatrics; and 1 each from Mental Health, Pharmacy, Preventive Medicine, SDS, Urology, and 5E). The most prevalent adverse events involved the anti-infective agents (n=16; 28%), the psychotherapeutic agents (n=11; 19%), and the cardiovascular agents (n=10; 17%). The anti-infective agents continue to be the top medication class involved in the reported adverse events with dermatologic manifestations of the adverse events the top system involved.

One event was deemed preventable (dose-related) which involved a 76yo female who was hospitalized with a diagnosis of hypotension from antihypertensive medication most likely causing 3 episodes of syncope prior to admission. The patient was recently changed from *Plendil* 5mg daily to *Atacand* 16mg daily. The patient presented to the ER with a BP of 116/94 which decreased to 97/40 within 4 hours. The patient was admitted, the *Atacand* discontinued, and cardiac work-up was normal. The patient was discharged the next day with instruction to follow-up with her provider.

Two events were deemed moderate (severity scale = mild, moderate, severe, fatal) — (1) the case above and (2) a 57yo male hospitalized for atypical chest pain also noted to have bradycardia (HR 49-78) secondary to verapamil (verapamil discontinued and patient discharged next day after cardiac work-up).

MUR COMMITTEE REPORT, RHONDA EUSTICE, PHARMD

The Medication Use Review (MUR) Committee, with representatives from the medical staff, nursing, clinical pharmacy, and nutrition, recently reviewed the following Drug Use Evaluations at their meetings.

Urinary Tract Infections — March 2002

Purpose:

Levaquin (levafloxacin) use has increased for this indication.

Patient Population/Sample size:

Random sampling of 165 patients with a diagnosis of urinary tract infection (identified by ICD-9 code)
55 medical records/CHCS reviewed

Medical Departments Involved in the Study:

PACC
Family Practice
Internal Medicine
Emergency Room
Pediatrics

Conclusions:

- 41% of UTIs were treated with SMZ/TMP (*Bactrim, Septra*), the drug of choice.
- The PYXIS in the ER only stocks *Levaquin* 500mg which may account for patients receiving that dose instead of the recommended 250mg dose.
- Only one isolate was resistant to SMZ/TMP.
- The recommended duration of therapy for uncomplicated UTI is 3 days. Only 13% of the patients receiving antibiotics for UTIs were given 3 days (or less) of therapy.

COPD/Pneumovax Review — April 2002

Purpose:

To review compliance with *Pneumovax* vaccination in COPD patients

Patient Population/Sample size:

284 patients seen between 1 September 2001 to 28 February 2002 for COPD (identified by ICD-9 code)
106 records reviewed

CHART/CHCS Review	Apr02	Oct01	Apr01
Patients who received *Pneumovax*	46%	43%	47%
Patients who did not receive *Pneumovax*	54%	57%	53%

Telephone Survey	Apr02	Oct01	Apr01
Patients who received *Pneumovax*	NP	NP	70%
Patients who did not receive *Pneumovax*	NP	NP	30%

Conclusion:

- There is lack of documentation in the medical records when *Pneumovax* is given. A patient telephone survey was attempted for this review, but not completed as the reviewer was unable to contact many patients.
- There was no significant change in the percentage of COPD patients receiving *Pneumovax* per CHCS/chart review.
- Patient information material has been posted in the Disease Management Clinic, Internal Medicine Clinic, Family Practice Clinic, and Allergy & Immunization Clinic with recommendations for patients to ask their providers about adult immunizations.

Hypertension Review — May 2002

Purpose:

To determine if elevated BP readings are being addressed at routine appointments.

Patient Population/Sample Size:

All patients with a diagnosis of CAD or hyperlipidemia were identified (identified by ICD-9 code)
191 patient identified, 110 charts reviewed
Patients with Diabetes excluded

Services Included:

IMC
FPC

Methods:

1) Chart reviewed for screening BP at routine appointments
2) If BP >135/85, looked to see if BP was rechecked by provider
3) If BP >135/85, looked to see if elevated BP reading was addressed

Results:

Classification of BP at initial appointment screen or recheck if done

JNC VI Classification	# (%) Patients
Optimal	19 (17%)
Normal	16 (14%)
High normal	21 (19%)
Stage 1	33 (30%)
Stage 2	11 (10%)
Stage 3	4 (4%)

Conclusion:

- The majority (69%) of patients with high-normal BP did not have BP rechecked at the appointment.
- Only 8% of provider notes for patients with a BP >135/85 at routine Family Practice and Internal Medicine Clinic appointments had a comment about the blood pressure.
- The Committee recommended another review be conducted on patients identified with a diagnosis of Hypertension.

A Bit of History — Memorial Day

- Memorial Day, originally called Decoration Day, was officially proclaimed on 5 May 1868 by General John Logan, national commander of the Grand Army of the Republic.
- It was first observed on 30 May 1868 when flowers were placed on the graves of Union and Confederate soldiers at Arlington National Cemetery.
- In 1915, Moina Michael wrote her poem: *We cherish too, the Poppy red*
  That grows on fields where valor led,
  It seems to signal to the skies
  That blood of heroes never dies.
  She then conceived of an idea to wear red poppies on Memorial day in honor of those who died serving the nation during war.
- Waterloo, NY, was officially declared the birthplace of Memorial Day by President Lyndon Johnson in May 1966, chosen because the town had made Memorial Day an annual, community-wide event during which businesses closed and residents decorated the graves of soldiers with flowers and flags.
- In 1971, Congress declared Memorial Day a national holiday to be celebrated the last Monday in May.
- Many southern states (Texas, Alabama, Virginia, Georgia, Mississippi, North & South Carolina, Louisiana, and Tennessee) have an additional, separate day for honoring the Confederate war dead (usually called Confederate Memorial Day).

MCXE-PCC

17 March 2002

MEMORANDUM FOR Primary Care Careline medical and nursing staff who care for pediatric patients

SUBJECT: Alternating antipyretics - ibuprofen and acetaminophen - in children with fevers is not recommended

1. In short: **There are no safety or efficacy studies to support this practice!**

2. EFFICACY. Acetaminophen (Tylenol) and ibuprofen (Motrin, Advil) reduce temperature by the same mechanism of action. The "medical" reason often given to justify alternating antipyretics is that they reduce temperature differently and therefore work better together. They don't. No study, anecdotes aside, has been done to show that this combination is more effective than either alone in reducing temperature.

3. SAFETY. Both can be renal toxic and acetaminophen more so in dehydrated patients, often the children who are given antipyretics to have varying degrees of dehydration. Their toxicity is felt possibly to be synergistic and now a case report has been published documenting this synergistic nephrotoxicity in a 14 month old on both meds. Acetaminophen's hepatotoxicity is also increased in dehydrated patients.

Parents were asked in one article how they "alternated" these two meds. Many dosing or better said "overdosing" regimens were quoted. Ibuprofen is a q 6-8 h med while acetaminophen is a q 4-6 h med. Some parents were giving one or the other up to every 2 hours.

And remember ibuprofen is not indicated below the age of 6 months for the treatment of fever.

4. FEVER PHOBIA. Instead of reinforcing a parent's fever phobia by giving them two antipyretics for their child, have them give only one and take a moment to allay their fever phobia as best you can.

5. In summary please do not prescribe alternating antipyretics or recommend that parents alternate these two medications. If they state they are already doing this ask them to use only one.

Continued on reverse side

Enclosure 1

6. References:

a. Mayoral, C, Alternating Antipyretics: Is This an Alternative?, *Pediatrics*, May 2000

b. Del Vecchio, M, Alternating Antipyretics: Is This an Alternative?, letter, *Pediatrics*, November 2001

c. Crocetti, M, Fever Phobia Revisited: Have Parental Misconceptions About Fever Changed in 20 Years?, *Pediatrics*, June 2001

d. Committee on Drugs - AAP, Acetaminophen Toxicity in Children, *Pediatrics*, October 2001

// original signed //
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